

§Appl. No. 09/889,227
Amdt. dated October 25, 2006
Reply to Office Action of, May 25, 2006

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-\text{NH}-\text{C}(\text{O})-\text{NH}-$,

A is a substituted moiety of the formula:



wherein L is phenyl, optionally substituted by halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of C_1 - C_5 linear or branched alkyl, C_1 - C_5 linear or branched haloalkyl up to perhaloalkyl and C_1 - C_3 alkoxy L^1 is selected from pyridinyl substituted by $-\text{C}(\text{O})\text{R}_x$, and

optionally substituted with 1-3 additional substituents independently selected from the group consisting of R^7 and halogen;

wherein R_x is NR_aR_b and R_a and R_b are

A) independently

- a) hydrogen,
- b) C_1 - C_{10} alkyl,
- c) C_6 aryl,
- d) pyridinyl
- e) substituted C_{1-10} alkyl,

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- f) substituted C₆ aryl,
- g) substituted pyridinyl
- h) -phenylpiperazine(pyridinyl),
- i) -phenylmorpholinyl,
- j) -ethylmorpholinyl,
- k) -ethylpiperidyl,
- l) -methyl pyrrolidinyl,
- m) -methyl tetrahydrofuryl,
- or
- n) -C₂H₄NH(phenyl);

where when R_a and R_b are a substituted group, they are substituted by

- a) halogen up to per halo,
- b) hydroxy,
- c) -N(CH₃)₂,
- d) C₁-C₁₀ alkyl,
- e) C₁-C₁₀ alkoxy,
- f) halosubstituted C₁₋₆ alkyl, or
- g) -OSi(Pr-i)₃; or

B) R_a and R_b together form piperazine or a substituted piperazine with substituents selected from the group consisting of

- a) halogen,
- b) hydroxy,
- c) C₁₋₁₀ alkyl,
- d) pyridinyl
- e) C₁₋₁₀ alkoxy,

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- f) C₆ aryl,
- h) g) halo substituted C₆ aryl, and
- i) h) N-(4-acetylphenyl);

M is selected from the group consisting of oxygen and sulfur;
and

B is
phenyl, substituted with 1-3 substituents independently selected from the group consisting of
halogen and R⁷,
and R⁷ is

- (a) C₁-C₆ linear or branched alkyl, optionally substituted with 1-3 halogen substituents; or
- (b) C₁-C₆ linear or branched alkoxy.

2. (Canceled)

3. (Previously Presented) A compound as in claim 1 wherein M is oxygen .

4. (Previously Presented) A compound as in claim 1 wherein the cyclic structures of B and L
bound directly to D are substituted in the ortho position by hydrogen.

5. (Canceled)

6. (Currently Amended) A compound of claim 1 wherein B of Formula I is phenyl,
substituted with 1-3 substituents independently selected from the group consisting of ~~halogen~~
chlorine, C₁-C₆ alkoxy or up to per halo substituted C₁-C₆ alkyl.

7. (Currently Amended) A compound of claim 3 wherein B of Formula I is

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phenyl, substituted with 1-3 substituents independently selected from the group consisting of ~~halogen~~
chlorine, C₁-C₆ alkoxy, or substituted C₁-C₆ alkyl, substituted by one or more halogen substituents.

8. **(Currently Amended)** A compound of claim 4 wherein B of Formula 1 is phenyl, substituted 1 to 3 times by 1 or more substituents selected from the group consisting of ~~halogen~~
chlorine, C₁-C₆ alkoxy or up to per halo substituted C₁-C₆ alkyl.

9. **(Previously Presented)** A compound of claim 1, wherein L is phenyl, optionally substituted by halogen up to perhalo.

10. **(Previously Presented)** A compound of claim 1, wherein L is phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of halogen and C₁-C₃ alkoxy.

11. **(Canceled)**

12. **(Canceled)**

13. **(Canceled)**

14. **(Canceled)**

15. **(Canceled)**

16. **(Canceled)**

17. **(Canceled)**

18. **(Previously Presented)** A compound of claim 4, wherein M is -O- .

19. **(Previously Presented)** A compound of claim 8 wherein M is -O-.

20. **(Previously Presented)** A compound of claim 9 wherein M is -O-.

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21. **(Previously Presented)** A compound of claim 10 wherein M is -O- .
22. **(Previously Presented)** A compound of claim 1 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₆ alkyl, halogen and C₁-C₆ alkoxy.
23. **(Previously Presented)** A compound of claim 3 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₆ alkyl, halogen and C₁-C₆ alkoxy.
24. **(Previously Presented)** A compound of claim 18 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₆ alkyl, halogen and C₁-C₆ alkoxy.
25. **(Previously Presented)** A compound of claim 19 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₆ alkyl, halogen and C₁-C₆ alkoxy.
26. **(Previously Presented)** A compound of claim 20 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₆ alkyl, halogen and C₁-C₆ alkoxy.
27. **(Previously Presented)** A compound of claim 21 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C₁-C₆ alkyl, halogen and C₁-C₆ alkoxy.

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28. (Canceled)

29. (Canceled)

30. (Canceled)

31. (Canceled)

32. (Canceled)

33. (Previously Presented) A compound of claim 3 wherein R_a and R_b are independently hydrogen or C_1 - C_6 alkyl.

34. (Previously Presented) A compound of claim 18 wherein R_a and R_b are independently hydrogen or C_1 - C_6 alkyl.

35. (Previously Presented) A compound of claim 19 wherein R_a and R_b are independently hydrogen or C_1 - C_6 alkyl.

36. (Previously Presented) A compound of claim 20 wherein R_a and R_b are independently hydrogen or C_1 - C_6 alkyl.

37. (Previously Presented) A compound of claim 21 wherein R_a and R_b are independently hydrogen or C_1 - C_6 alkyl.

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38. (Previously Presented) A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-\text{NH}-\text{C}(\text{O})-\text{NH}-$,

A is of the formula: $-\text{L}-\text{M}-\text{L}^1$, wherein

L is phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1 - C_5 linear or branched alkyl, C_1 - C_5 linear or branched haloalkyl up to perhalo, C_1 - C_3 alkoxy and halogen;

L^1 is pyridinyl, substituted by $-\text{C}(\text{O})\text{R}_x$;

wherein R_x is NR_aR_b and R_a and R_b are independently

hydrogen,

C_1 - C_{10} alkyl,

C_6 aryl,

pyridinyl, substituted C_{1-10} alkyl,

substituted C_6 aryl, or

substituted pyridinyl,

where R_a and R_b are a substituted group, they are substituted by halogen up to per halo; and

M is selected from the group consisting of oxygen and sulfur

and

B is phenyl, substituted with 1-3 substituents independently selected from the group consisting of R^7 and halogen;

and R^7 is

(a) C_1 - C_6 linear or branched alkyl, optionally substituted with 1-3 halogen substituents; or

(b) C_1 - C_6 linear or branched alkoxy.

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39. (Previously Presented) A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is $-\text{NH}-\text{C}(\text{O})-\text{NH}-$,

A is of the formula: $-\text{L}-\text{M}-\text{L}^1$,

L is phenyl,

M is $-\text{O}-$,

L^1 is pyridinyl substituted by $-\text{C}(\text{O})\text{R}_x$,

wherein R_x is NR_aR_b and R_a and R_b are independently
hydrogen,

$\text{C}_1\text{-C}_{10}$ alkyl,

C_6 aryl,

pyridinyl,

substituted C_{1-10} alkyl,

substituted C_6 aryl, or

substituted pyridinyl

where R_a and R_b are a substituted group, they are substituted by halogen up to per halo,
and

B is a phenyl group substituted by trifluoromethyl or tert-butyl, and optionally additional
substituents selected from the group consisting of halogen up to per halo, and W_n where n is 0-3, and
each W is independently selected from the group consisting of

$\text{C}_1\text{-C}_{10}$ alkyl,

$\text{C}_1\text{-C}_{10}$ alkoxy,

C_6 aryl,

pyridinyl,

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and substituted C₁-C₁₀ alkyl, substituted by one or more substituents independently selected from the group consisting of halogen up to per halo.

40. (Previously Presented) A compound as in claim 38 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen.

41. (Canceled)

42. (Previously Presented) A compound as in claim 39 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen.

43. (Canceled)

44. (Previously Presented) A compound as in claim 38 wherein substituents for B, are selected from the group consisting of up to per halo substituted C₁-C₆ alkyl and halogen.

45. (Previously Presented) A compound as in claim 39 wherein the optional substituents for B are selected from the group consisting of up to per halo substituted C₁-C₆ alkyl and halogen.

46. (Canceled)

47. (Canceled)

48. (Canceled)

49. (Canceled)

50. (Previously Presented) A pharmaceutically acceptable salt of a compound of formula I of claim 1 which is

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a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

51. (Cancelled)

52. (Canceled)

53. (Previously Presented) A pharmaceutically acceptable salt of a compound of claim 38 which is

a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

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54. (Previously Presented) A pharmaceutically acceptable salt of a compound of claim 39 which is

a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

55. (Previously Presented) A pharmaceutical composition comprising a compound of claim 1 or a pharmaceutically acceptable salt of a compound of formula I, and a physiologically acceptable carrier.

56. (Canceled)

57. (Canceled)

58. (Previously Presented) A pharmaceutical composition comprising a compound of formula I of claim 38 or a pharmaceutically acceptable salt thereof, and a physiologically acceptable carrier.

59. (Previously Presented) A pharmaceutical composition comprising a compound of formula I of claim 39 or a pharmaceutically acceptable salt thereof, and a physiologically acceptable carrier.

60. (Canceled)

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61. (Cancelled)

62. (Currently Amended) A method for inhibiting the enzyme raf kinase in a human or animal, comprising administering a pharmaceutically acceptable amount of a compound of Formula I of claim 1 to said mammal.

63. (Canceled)

64. (Currently Amended) A method for inhibiting the enzyme raf kinase in a human or animal, comprising administering a pharmaceutically acceptable amount of a compound of Formula I of claim 38 to said mammal.

65. (Currently Amended) A method for inhibiting the enzyme raf kinase in a human or animal, comprising administering a pharmaceutically acceptable amount of a compound of Formula I of claim 39 to said mammal.

66. (Canceled)

67. (Canceled)

68. (Previously Presented) A compound of claim 1 wherein the optional substituents on L¹ are selected from the group consisting of methyl, trifluoromethyl, methoxy, Cl and F.

69. (Previously Presented) A compound of claim 1 wherein the substituents of B and L are independently selected from the group consisting of methyl, trifluoromethyl, tert-butyl, methoxy, Cl, and F.

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70. (Currently Amended) A pharmaceutical composition ~~for the treatment of a cancerous cell growth~~ comprising a compound of formula I of claim 1 or a pharmaceutically acceptable salt of a compound of formula I and a physiologically acceptable carrier.

71. (Previously Presented) A compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of the formula: -L-M-L¹,

wherein L is phenyl, optionally substituted with substituents independently selected from the group consisting of halogen, C₁-C₅ alkyl, C₁-C₅ alkyl substituted by halogen and C₁-C₅ alkoxy;

L¹ is pyridinyl, substituted with -C(O)NR^aR^b and optionally substituted with one or two substituents selected from the group consisting of R⁷, OR⁷ and halogen, wherein R⁷ is hydrogen, C₁-C₅ alkyl or C₁-C₅ alkyl substituted by halogen,

wherein R^a and R^b independently are

- a) hydrogen or
- b) C₁-C₅ alkyl;

B is phenyl, substituted by tert-butyl or trifluoromethyl and optionally substituted with additional substituents independently selected from the group consisting of

- a) halogen,
- b) C₁-C₅ alkyl substituted by halogen or
- c) C₁-C₄ alkoxy.

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72. (Currently Amended) A pharmaceutical composition ~~for the treatment of a cancerous cell growth~~ as in claim ~~71~~ 70 wherein the pharmaceutically acceptable salt is

a) a basic salt of an organic acid or an inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

73. (Canceled)

74. (Canceled)

75. (Canceled)

76. (Canceled)

77. (Canceled)

78. (Canceled)

79. (Canceled)

80. (Canceled)

81. (Canceled)

82. (Canceled)

83. (Canceled)

84. (Canceled)

85. (Canceled)

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- 86. (Canceled)
- 87. (Canceled)
- 88. (Canceled)
- 89. (Cancelled)